41. The process of claim 35, wherein the polypeptide is a TNF-α.

42. The process of claim 12, wherein the cytokine is a TNF-α.--

REMARKS

Reconsideration and continuing examination of the above-identified application is respectfully requested in view of the amendments above and the discussion that follows.

Claims 17 and 30 have been cancelled. Claims 1, 2, 8, 12, 13, 18, 26, 27, 29, 31 and 36 have been amended and claims 37-42 have been added. The Action noted that claims 1-3, 6, 8-14, 17-21 and 26-36 are pending in the application. However, it is believed that claim 22 is still present in the application, and its above omission was an inadvertent error. It is therefore believed that claims 1-3, 6, 8-14, 18-22, 26-29 and 31-42 are in the case and are before the Examiner.

I. The Amendments

Claims 1, 2, 12, 13, 18, 26, 27, 29 and 36 have been amended for added clarity so that the word "gene" is replaced by the words "nucleic acid". In addition, the clarifying phrase "to produce the radiosensitizing factor" has been added to claim 1 to further describe the polypeptide encoded by the nucleic acid. This language is supported at least by the disclosures at page 9, lines 9-12.

The amendments to claim 29 are supported by the specification at least, for example, at page 16, line 28 through

page 18, line 21, as well as at least by claims 8, 10, 26 and 30. Claim 31 has been amended by canceling the word "increasing", and replacing it with the word "expressing". Reference to cancelled claim 30 has also been removed.

Support for new claim 37 can be found in the specification at least at, for example, page 11, lines 11-26, whereas support for new claims 38-42 can be found in the specification at least, for example, in Example VI and in original claims 2, 3, 5 and 16.

Accordingly, no new matter has been added by way of these amendments.

A marked up copy of amended claims is provided at the end of this paper.

II. Rejections Under 35 U.S.C. §112, Second Paragraph

Claims 1-3, 6, 8-14, 17-21 and 26-36 were rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. The claims are said to be vague in the use of the term "gene" and "increasing." Although it cannot be agreed that the claims were indefinite, amendments have been provided to remove the term "gene" and replace it with the phrase "nucleic acid." Amendments also have been provided to remove the term "increasing." It is therefore believed that these rejections are moot, and withdrawal of the rejections is requested.

Claims 8 and 36 were rejected for alleged lack of antecedent basis. Although the basis for this rejection can also not be agreed with, amendments have been provided that are thought to also make these rejections moot. Withdrawal of the rejections is therefore requested.

Claim 36 also was rejected as allegedly lacking an active step to correlate with the preamble. This basis for rejection is respectfully traversed.

The preamble of claim 36 recites a "method of assessing the response of a cell". Part (d) of claim 36 recites "assessing the response of said cell." That assessment clearly constitutes the sort of "active step" the Action deems required.

Moreover, the "criteria" under which assessing would be performed would easily be understood by one of skill in the art after reviewing the specification. For example, page 15, lines 22-33, lists a number of genes induced by ionizing radiation, the expression of which can be used to assess a cellular response. In addition, the ability of ionizing radiation to damage or kill a cell provides a suitable point of assessment for both radiosensitizing and radioprotective agents. Pages 22-23. Thus, it is submitted that the recited step of "assessing" both satisfies the preamble and clearly identifies the subject matter to be claimed. Withdrawal of the rejection is therefore respectfully requested.

III. Rejections Under 35 U.S.C. §102

Claims 29 and 30 were rejected under §102(e), §102(a) and §102(b) over Zhang *et al.*, Walther *et al.*, and Uzvolgyi *et al.*, respectively. These bases for rejection are respectfully traversed. However, in the interest of advancing the prosecution, the rejected claims have been amended and cancelled, respectively.

More specifically, none of the relied-on teachings discloses or suggests a pharmaceutical composition comprising a genetic construct that comprises a nucleic acid sequence that

encodes a TNF-α operatively linked to a constitutive promoter, wherein the genetic construct is packaged within an adenovirus particle, as required by amended claim 29. Thus, claim 29 is directed to novel subject matter in view of the cited art, and each of the rejections against the claim under §102 should be withdrawn.

Moreover, those teachings do not support a Section 103 rejection of the amended claim. This is the case particularly in view of the "rapid decrease" in p53 gene expression observed using the adenoviral vector disclosed in the Zhang '290 patent (see, e.g., column 14, lines 30-35). The Examiner's attention is also invited to the successful transfection, and subsequent growth inhibition of human cancer cells transduced with retroviral vectors encoding genes such as Rb and TNF-α that are reported in the Uzvolgyi et al. disclosure at page 299, col. 1, last paragraph, and the Walther et al. disclosure at page 1565, Abstract. It is thus submitted that claim 29 is novel and also would not have been obvious to a worker of ordinary skill at the time of the invention. This basis for possible rejection should therefore not be asserted and claim 29 and its dependent claims should therefore be patentable.

IV. Summary

Claim 30 has been cancelled. Claims 1, 2, 8, 12, 13, 18, 26, 27, 29, 31 and 36 have been amended and claims 37-42 have been added. Each basis for rejection has been dealt with and made moot or otherwise overcome.

It is therefore believed that the application is in condition for allowance. An early notice to that effect is earnestly solicited.

Check No. 077913 in the amount of $460.00 is enclosed to cover the cost of the one new independent claim that is in excess of those independent claims already paid for. No further fee is believed needed for the other new claims in view of the claims that have been cancelled.

No further fee or petition is believed to be necessary. However, should any further fee be needed, please charge our Deposit Account No. 23-0920, and deem this paper to be a required petition.

The Examiner is requested to phone the undersigned should any questions arise that can be dealt with over the phone to expedite this prosecution.

It is noted that a Revocation and Power of Attorney document is enclosed with this Reply.

Respectfully submitted,

By _____

Edward P. Gamson, Reg. No. 29,381

Enclosures
Revocation and Power of Attorney
Petition and fee
Added independent claim fee

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CERTIFICATE OF MAILING

I hereby certify that this Reply, the Petition for Extension of Time and its fee, the Revocation and Power of Attorney and the added claim fee are being deposited with the United States Postal Service with sufficient postage as First Class Mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231 on November 7, 2002.

Edward P. Gamson

MARKED UP COPY OF AMENDED CLAIMS

Please amend claims 1, 2, 8, 12, 13, 18, 26, 27, 29, 31 and 36 as follows:

1. (Three times amended) A process of treating a human cancer patient comprising providing to a cancer cell in said patient a [gene] nucleic acid encoding a radiosensitizing polypeptide operatively linked to a constitutive promoter and contacting said cell with ionizing radiation, whereby the [gene] nucleic acid is expressed to produce the radiosensitizing polypeptide and the cancer is treated.

2. (Twice Amended) The process of claim 1, wherein the nucleic acid encodes [gene is] a TNF-α [gene].

8. (Twice Amended) The process of claim 1, wherein [the transfection is] said nucleic acid is provided by transfection by liposomes, adenovirus or HSV-1.

12. (Amended) A process of sensitizing a cell to the effects of ionizing radiation comprising transfecting the cell with an adenovirus vector construct comprising a [gene] nucleic acid that encodes a cytokine, wherein said cytokine is synthesized in and secreted from said cell.

13. (Amended) The process of claim 12, wherein the nucleic acid that encodes the cytokine [gene] is positioned under control of a promoter other than an adenovirus promoter.

18. (Amended) A process of radioprotecting a cell from the effects of ionizing radiation comprising:

(a) obtaining a genetic construct comprising a [gene] nucleic acid encoding a cell radioprotecting factor operatively linked to a constitutive promoter; and

(b) transfecting a cell with the genetic construct; whereby said radioprotecting factor is expressed and said cell is protected from said effects.

26. (Amended) A process of radioprotecting a cell from the effects of ionizing radiation comprising transfecting the cell with an adenovirus vector construct comprising a [gene] nucleic acid encoding a radioprotecting factor in a mammalian cell.

27. (Amended) The process of claim 26, wherein the [gene] nucleic acid is positioned under control of a promoter other than an adenovirus promoter.

29. (Amended) A pharmaceutical composition comprising a genetic construct comprising a [gene] nucleic acid that encodes a [cell radiosensitizing or radioprotecting factor] TNF-α operatively linked to a constitutive promoter dispersed in a pharmacologically acceptable carrier, wherein the genetic construct is packaged within an adenovirus particle.

31. (Amended) A method of [increasing the level of] expressing a radioprotecting or radiosensitizing factor in a

mammal comprising administering to the mammal an effective amount of the pharmaceutical composition of claim 29 [or claim 30].

36. (Amended) A method of assessing the response of a cell to the constitutive production of radiosensitizing or radioprotecting factors following ionizing radiation comprising:

(a) growing the cell in culture

(b) transfecting the cell with a genetic construct comprising a [gene] nucleic acid that encodes the cell radiosensitizing factor or radioprotecting factor operatively linked to a constitutive promoter, whereby said [polypeptide] nucleic acid is expressed to produce the radiosensitizing factor or radioprotecting factor;

(c) exposing the cell to an effective dose of ionizing radiation; and

(d) assessing the response of the cell.

Please add new claims 37 through 41 as follows:

--37. The pharmaceutical composition of claim 29, wherein the adenovirus particle contains a deletion of the E1 region and/or the E3 region of the adenoviral genome.

38. A process of inhibiting growth of a tumor in a host comprising the steps of:

(a) injecting into the tumor a therapeutically effective amount of the pharmaceutical composition of claim 29, and

(b) administering to the host an effective dose of ionizing radiation, whereby the growth of the tumor is inhibited by expression of the nucleic acid encoding a TNF-α and the administration of ionizing radiation.

39. The process of claim 38, wherein the amount of the pharmaceutical composition is between $10^8$ and $10^{11}$ plaque forming units.

40. The process of claim 38, wherein the dose of ionizing radiation is between 50 and 70 Gray.

41. The process of claim 35, wherein the polypeptide is a TNF-α.

42. The process of claim 12, wherein the cytokine is a TNF-α.--